

## **REMARKS**

Reconsideration of the application, as amended, is respectfully requested. The Applicants wish to draw the Examiner's attention to the applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof. Office actions have already issued on many of the listed cases. In particular, the Applicant wishes to draw the Examiner to co-pending continuation-in-part application No. 10/153,483, filed May 22, 2003.

The Applicants note that the Examiner did not return the executed PTO 1449 form for the 8<sup>th</sup> Supp. IDS that was mailed on May 14, 2003. Subsequent to the issuance of this Office action, the Applicants had filed a 9<sup>th</sup> Supp. IDS. Attached copies of PTO stamped post-cards show that the Patent Office did receive both IDSs, PTO-1449 forms and cited references. The Applicants request that the Examiner fully execute the PTO 1449 forms for the 8<sup>th</sup> and 9<sup>th</sup> Supp. IDSs and return a copy of the executed PTO 1449 forms to the undersigned representative. Copies of the 8<sup>th</sup> and 9<sup>th</sup> Supplemental IDSs and associated PTO 1449 forms are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

Claims 1-35 were pending in this application. The claims are amended as noted above. Claims 1, 2, 20-31, and 35 are canceled without prejudice to their future filing, as they are drawn to restricted and non-elected subject matter. Claims 5-8 and 10 are amended to remove dependency on withdrawn claims, and serve merely to clarify the claim language. Claims 11-19 are amended and are drawn to methods of making core/shell nanoparticles. Particularly claim 11 is amended to add the steps of core/shell particle synthesis and isolation, and remove dependency on claim 3. These amendments merely clarify the subject matter of the claims. Claim 32 is amended to recite the phrase "wherein the nanoparticle core is magnetic" in order to clarify the subject matter and language of the claim. New claim 36 is a product by process claim, based on the novel core/shell particles produced by the method of claim 11. All of the above claim amendments do not constitute new matter, and are fully supported in the application as filed. Claims 3-19, and 32-34 are pending in this application.

Turning now to the Office action, the Examiner asserted that the priority dates for claims 6-9 and 32-34 can only extend to the filing date of the application, specifically December 28, 2001. Applicants respectfully traverse this assertion. The provisional

application 60/293,861, filed May 25, 2001 discloses and recognizes the broad utility of the claimed core/shell nanoparticle conjugates. This utility includes the tailorability of the physical properties of the core/shell nanoparticles through the use of a variety of biomolecules and nanoparticle cores that can be chosen depending on the particular desired properties, as disclosed, for example, on the last page of the specification. Thus, Applicants respectfully assert that the entirety of the claims are entitled to the filing date (May 25, 2001) of the provisional application.

The Examiner also objected to the drawings under 37 CFR 1.83(a). Applicants file herewith replacement (formal) drawings 1-6 to correct the asserted deficiencies of the originally filed figures, as recited in the Office action. The description of the various modifications introduced by the replacement Figures are presented above. Accordingly, the Applicants submit that the drawing objection has been overcome.

Regarding the specification, the Examiner objected to certain informalities in citations. The specification was amended in order to replace the PCT application numbers with the WO publication numbers. Further the description for Figure 6 is amended to incorporate the reference letters A, B, and C, and includes their significance to the Figure. Accordingly, the Applicants submit that the specification objection has been overcome.

The Examiner objected to claims 11-19 under 37 CFR 1.75(c) as allegedly improperly dependent for failing to further limit a previous claim. As filed, claim 11 depended from claim 3 and allegedly failed to recite a limitation to the claimed nanoparticle oligonucleotide conjugate of claim 3. Claims 11-19 are amended as noted above, in order to recite methods of making the claimed nanoparticle oligonucleotide conjugates. Claim 11 is also amended to replace the semicolon located at the end of the claim with a period. Accordingly, Applicants believe that the claim objections are rendered moot.

#### I. Claim Rejections under 35 USC § 112

Claims 32-34 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite for failing to point out and particularly claim the subject matter regarded as the invention. Specifically, claim 32 is alleged indefinite for the recitation of the dependency on the nanoparticle conjugate of claim 2, and for reciting a step (b) where

a magnetic field is used to accelerate movement of the nanoparticle conjugate to the surface. Applicants respectfully traverse the rejection.

Claim 32 is amended as noted above. These amendments merely clarify the dependency and language of the claim, and should not be viewed as limiting the scope of the originally claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.

## II. Claim Rejections under 35 USC § 102

Claims 3-5, 7, and 10-16 stand rejected under 35 U.S.C. § 102(e), alleged to be anticipated by Abbott et al. (U.S. Patent 6,277,489) (“Abbott”). Specifically, Abbott is alleged to teach a multilayered material comprising a particulate substrate, a metal film layered onto the substrate, and a recognition moiety attached to the metal layer. Further the particulate substrate is alleged to be any size. The Applicants respectfully traverse the rejection.

Under MPEP § 2131, “(a) claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference” (citing *Verdegaal Bros v. Union Oil Co. of California*, 814 F.2d 628, 631). MPEP § 2131.

The teachings of Abbott fail to teach the elements of the instant invention as claimed. Claim 3 is drawn to a core/shell nanoparticle oligonucleotide conjugate comprising an inner metal-containing nanoparticle core; an outer non-alloying gold shell surrounding the nanoparticle core; and oligonucleotides attached to the gold shell. Abbott does not teach a non-alloying gold shell metal coating. As described in the specification of the instant application, the core/shell nanoparticle conjugate of the invention retains the physical and/or optical properties of the core with no observed physical or optical competing effects from the non-alloying gold shell. Prior to the instant invention, such core/shell nanoparticles were unknown and desirable.

A major advance would be to devise a method for designing particles with physical properties of a chosen nanoparticle composition but the surface chemistry of gold.  
(specification p. 2, ln. 4-5)

In yet another aspect the present invention provides a method for preparation of non-alloying gold core/shell nanoparticles and product produced therefrom. The method of the invention comprises providing an inner nanoparticle core, treating the core simultaneously with a solution comprising a gold salt and a solution comprising a reducing agent, and isolating the core/shell nanoparticles. *The method provides for the first time a non-alloying gold shell surrounding a nanoparticle core. These non-alloying gold core/shell nanoparticles exhibit surprising superior spectroscopic properties not found in conventional gold core/shell nanoparticles and can be functionalized with molecules such as nucleic acids and receptors, to produce nanoparticle conjugates that can be used for targeting and detecting target analytes such as nucleic acids, antigens, proteins, carbohydrates and other substances.*

(specification p.4, ln.32 - p.5, ln.8)

Thus, the non-alloying gold shell provides a convenient surface for the attachment of specific binding substances that, in claim 3, are oligonucleotides, while the core particle retains its desirable physical and/or optical properties. Prior core/shell particles suffered from losses in the physical and/or optical properties of the core particle and/or the shell (see e.g., Example 1 pp. 9-14, providing an embodiment of the invention with Ag core and Au shell). Abbott is completely silent with respect to any non-alloying gold core/shell nanoparticle and therefore fails to anticipate the invention as claimed.

Regarding the product-by-process claims discussed in the Office action (at page 6), the claims at issue (11-16) are amended as noted above. New claim 36 is drafted as a product-by-process claim based on the novel core/shell particles produced by the method of claim 11. Thus, claim 36 does not suffer from the alleged defect in the prior product-by-process claims.

Accordingly, Applicants respectfully submits that withdrawal of the rejection of the claims under 35 U.S.C. § 102(e) based on Abbott is in order and is respectfully requested.

### III. Claim Rejections under 35 USC § 103

Claims 8-9 and 32-34 stand rejected under 35 U.S.C. § 103(a), alleged as unpatentable over Abbott (cited above), in view of Mirkin et al. (US 6,361,944) ("Mirkin"). More specifically, Abbott is re-alleged as above while Mirkin is alleged to teach nanoparticle-oligonucleotide conjugates used in detection of nucleic acids, wherein the

nanoparticles are magnetic, including cores of  $\text{Fe}_3\text{O}_4$  with a silica shell, conjugated to oligonucleotides. Mirkin is further alleged to teach nanoparticle-oligonucleotide conjugates in hybridization methods, including methods for detection on a surface. It is asserted that it would be obvious to one of skill in the art to use the magnetic core of Mirkin in the particles of Abbott, motivated by the desire for easy separation of magnetic particles having hybridized targets from a test solution. Applicants respectfully traverse the rejection.

In order to establish a prima facie case of obviousness, there must exist 1) a suggestion or motivation, either in the cited references or general knowledge of one of skill in the art, to modify or combine reference teachings; 2) a reasonable expectation of success; and 3) the cited art references must teach or suggest all the claim limitations. M.P.E.P. § 2143.

The failure of Abbott to teach or suggest all the claim limitations is discussed above in section II. Even assuming, *arguendo*, that Mirkin does teach, as alleged, nanoparticle-oligonucleotide conjugates used in detection of nucleic acids, wherein the nanoparticles are magnetic, including cores of  $\text{Fe}_3\text{O}_4$  with a silica shell, conjugated to oligonucleotides, and such conjugates in hybridization methods, including methods for detection on a surface, such a disclosure does not cure the deficiencies of Abbott. Moreover, even if the alleged cores of Mirkin are combined with the disclosure of Abbott as the Examiner would have it, one of skill would not arrive to the claimed nanoparticle core/shell oligonucleotide conjugates, as claimed. Accordingly, Applicants respectfully submit that withdrawal of the rejection of the claims under 35 U.S.C. § 103(a) based on the combination of Abbott with Mirkin is in order and is respectfully requested..

IV. Conclusion

In light of the above arguments, the Examiner is respectfully requested to reconsider the application as claimed. If the Examiner believes that a telephonic or personal interview would expedite prosecution of the application, she is invited to contact the undersigned at (312) 913-0001.

Respectfully submitted,



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Emily Miao

Registration No. 35,285

Date: December 15, 2003

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 01-661-A)

In the Application of:

Chad A. Mirkin, et al.

Serial No.: 10/034,451

Filed: December 28, 2001

For: NON-ALLOYING CORE SHELL  
NANOPARTICLES

Examiner: T. Strzelecka

Group Art Unit: 1637

Confirmation No. 9317

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**COPY**

**EIGHTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies<sup>1</sup> of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. Heller, et al., U.S. Patent No. 4,966,143 issued 02/26/91
2. Kausch, et al., U.S. Patent No. 5,508,164 issued 04/16/96
3. Ewart, et al., U.S. Patent No. 5,922,537 issued 07/13/99
4. An, et al., U.S. Patent No. 5,972,615 issued 10/26/99
5. Blackburn, et al., U.S. Patent No. 6,264,825 issued 07/24/01

<sup>1</sup>To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated there between; if no such English language equivalent is cited, then none is known to undersigned.

6. Yguerabide, et al., U.S. Patent No. 6,214,560 issued 04/10/01
7. International Patent WO 94/29484 published 12/22/94
8. International Patent WO 00/25136 published 05/04/00
9. Mohanty J., et al., "Pulsed laser excitation of phosphate stabilized silver nanoparticles," *Proc. Indian Acad.*, Vol. 112, No. 1, p. 63-72 (2000)
10. Nicewarner- Peña S., et al., "Hybridization and Enzymatic Extension of Au Nanoparticle-Bound Oligonucleotides," *J. Am. Chem. Soc.*, Vol. 124, p. 7314-7323 (2002)
11. Whitesides G.M., et al., "Soft Lithography in Biology and Biochemistry," *Annu. Rev. Biomed. Eng.*, p. 335-373 (2001)

In accordance with MPEP Sections 609 and 707.05(b), it is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art



consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,

Dated: 5/14/03



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FORM PTO-1449  
(Rev. 2-32)

U.S. Department of Commerce  
Patent and Trademark Office

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01-661-A

Serial N .

10/034,451

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Chad A. Mirkin, et al.

Filing Date:

December 28, 2001

Group:

1645

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	1.	4,996,143	02/26/91	Heller, et al.	435	6	04/13/90
	2.	5,508,164	04/16/96	Kausch, et al.	435	6	10/29/93
	3.	5,922,537	07/13/99	Ewart, et al.	435	6	11/8/96
	4.	5,972,615	10/26/99	An, et al.	435	6	01/21/98
	5.	6,264,825	07/24/01	Blackburn, et al.	205	777.5	06/23/99
	6.	6,214,560	04/10/01	Yguerabide, et al.	435	7.1	04/18/97

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	7.	WO 94/29484	12/22/94	PCT				
	8.	WO 00/25136	05/04/00	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).

	9.	Mohanty J., et al. "Pulsed laser excitation of phosphate stabilized silver nanoparticles," <i>Proc. Indian Acad. Sci.</i> , Vol. 112, No. 1, p. 63-72.
	10.	Nicewarner- Peña S., et al., "Hybridization and Enzymatic Extension of Au Nanoparticle-Bound Oligonucleotides," <i>J. Am. Chem. Soc.</i> , Vol. 124, p. 7314-7323 (2002)
	11.	Whitesides G.M., et al., "Soft Lithography in Biology and Biochemistry," <i>Annu. Rev. Biomed. Eng.</i> , p. 335-373 (2001)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.

Hon. Commissioner of Patents and Trademarks

S/N—10/034,451

Atty EM

Re: Applicant - Mirkin, et al.

Case No. 01-661-A

**NON-ALLOYING CORE SHELL NANOPARTICLES**

Date Mailed: May 14, 2003

Sir:

Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of:

- ☒ Transmittal Letter
- ☒ Eighth Supplemental Information Disclosure Statement
- ☒ U.S. PTO 1449 Form with copies of 11 references
- ☒ Return Receipt Postcard



Fee Enclosed  
\$ 0.00

Respectfully,  
McDonnell Boehnen Hulbert & Berghoff  
Attorney for Applicant

EV333564745US

# PATENT

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<sup>1</sup>To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated there between; if no such English language equivalent is cited, then none is known to undersigned.

document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,



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Dated: 7/8/03

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U.S. Department of Commerce  
Patent and Trademark Office

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Atty. Docket No.

01-661-A

Serial N .

10/034,451

Applicant:

Chad A. Mirkin, et al.

Filing Date:

December 28, 2001

Group:

1645

U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
1.	6,180,415	01/30/01	Schultz et al.	436	518	02/20/98

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation Yes No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc).


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IER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if  
nformance and not considered. Include copy of this form with next communication.

Hon. Commissioner of  
Patents and Trademarks

S/N—10/034,451

Atty EM

Re: Applicant - Mirkin, et al.

Case No. 01-661-A

**NON-ALLOYING CORE SHELL NANOPARTICLES**

Date Mailed: July 8, 2003

Sir:

Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of:

- ☒ Transmittal Letter
- ☒ Ninth Supplemental Information Disclosure Statement
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Respectfully,  
McDonnell Boehnen Hulbert & Berghoff  
Attorney for Applicant

